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PhRMA

October 1, 2004

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: Docket No. 2004N-0242; Institutional Review Boards; Registration Requirements; 69 Federal Register 40556; July 6, 2004.

Dear Sir or Madam:

The Pharmaceutical Research and Manufacturers of America (PhRMA) welcomes the opportunity to comment on the above referenced proposed rule issued by the Food and Drug Administration (FDA). PhRMA represents the country's leading pharmaceutical research and biotechnology companies, which are devoted to inventing medicines that allow patients to live longer, healthier, and more productive lives. PhRMA members invested an estimated $33.2 billion in 2003 in discovering and developing new medicines. PhRMA companies are leading the way in the search for new cures.

PhRMA generally supports efforts which may enhance the processes surrounding Institutional Review Board (IRB) oversight of clinical trials and preservation of the rights and safety of clinical research human subjects. PhRMA views the concept of IRB registration as an opportunity to better identify IRBs involved in FDA-regulated clinical research, which may allow for more effective communication between FDA and IRBs.

Specific Comments

PhRMA submits the following comments on the proposed requirement for IRB registration and changes to FDA regulations at 21 C.F.R. Part 56:

A. IRB Registration (Proposed §56.106)

1. Who must Register? (Proposed §56.106(a))

PhRMA suggests that the rule clarify the scope of the requirement to include "non-local" or "commercial IRBs."

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In response to FDA's request for comment on whether there are circumstances in which foreign IRBs should be required or invited to register, PhRMA recommends that this rule not include foreign IRBs or Ethical Review Committees (ERCs). ERC registration should be allowed as a voluntary activity. While PhRMA acknowledges FDA's role in ensuring that the rights and welfare of clinical research human subjects are protected, for non-US subjects, this responsibility resides with the governments, authorities, institutions and clinical investigators in the countries in which the research is being conducted. The same paradigm should be applied to global studies where a single study involves multi-national sites, both US and non-US, i.e., IRB registration required for US sites only. However, voluntary registration is recommended to achieve one of FDA's stated purposes of registration which is to make educational and other information available to all IRBs/ERCs. HHS may benefit from feedback solicited directly from representative ERCs abroad.

2. What Information Must an IRB Provide When Registering? (Proposed §56.106(b))

- The proposed rule's limitation regarding qualifications for designation of the senior officer of the institution may be too restrictive, e.g., if the senior officer is an IRB member, this alone should not invalidate the registration. According to the current wording, it appears that if the individual designated as the senior officer did fall into one of the prohibited categories, the IRB could be open to enforcement action by FDA. Because such restrictions are not currently included within 21 C.F.R. Part 56 and are not germane to the stated goals of the proposed rule, PhRMA recommends changing the wording such that registration requires the identification of the institution's senior officer who has oversight responsibilities for the IRB's activities.

- Regarding accreditation, as 21 C.F.R. Part 56 has no requirement for accreditation, PhRMA recommends that this not be included as a registration requirement. Such information may be collected outside of a regulated process.

- PhRMA acknowledges that the Internet registration site may request more information from IRBs reviewing research conducted or supported by HHS than those reviewing clinical investigations regulated by FDA that are not conducted or supported by HHS. PhRMA suggests that registration information specifically requested for HHS-funded research be clearly delineated and marked as optional for IRBs uninvolved in HHS-funded research.

4. Where Can an IRB Register? (Proposed §56.106(d))

PhRMA recommends that FDA consider issuing an acknowledgement for IRBs that register electronically in order to document the registration process.

5. How Does an IRB Revise Its Registration Information (Proposed §56.106(e))?

PhRMA notes that the requirement for providing revised registration information within 30 days upon an IRB's review of new types of FDA-regulated products, as specified in the preamble, is not reflected in the proposed rule wording.

6. What happens if an IRB Does Not Register?

- FDA has requested comments on how best to ensure that all sponsors and investigators involved in clinical investigations using human subjects use only registered IRBs to review and approve those clinical investigations. PhRMA suggests that since sponsors use the Form FDA 1572 to notify FDA of new investigators, this form may be a useful tool to capture the IRB registration. Investigators must complete and sign this document and return it to the sponsor, who then forwards the document to FDA. Additionally, language can be added to the investigator's responsibilities, noted on the back page of the Form FDA 1572, that indicates the investigator's responsibility to comply with the required use of an FDA-registered IRB.

- PhRMA further requests that IND sponsors and investigators have access to the HHS electronic IRB registration database as they currently do for Federalwide Assurances. If it is not possible for sponsors and investigators to directly access the database, FDA or HHS should issue a report of IRB registrations or issue certificates to the individual IRBs.

- Written registration, as noted within the proposed rule, should remain an option for a predefined period of time in order to achieve maximum compliance.

- FDA has requested feedback to the question "What Sanctions or administrative mechanisms, if any, should be or might be used against sponsors and investigators who use unregistered IRBs?" PhRMA believes that it is unnecessary to develop strict sanctions to address non-compliance for an administrative requirement. PhRMA encourages FDA to adopt a flexible approach that minimizes obstacles which may hinder research, development or marketing of new therapies. PhRMA deems it inappropriate to create such sanctions against sponsors.

  FDA may consider developing an algorithm for handling IRB non-registration issues, escalating its approach in stages. For example, if a non-registered IRB is identified to FDA (perhaps via 1572 as proposed above), FDA may send a certified letter to the IRB, along with the forms and/or instructions for registration. If this approach fails to secure an adequate response, a telephone call to the investigational site could be the next step. Assuming that fails, an FDA visit to the IRB may be warranted. Such an escalation approach would allow

FDA to take appropriate action against a non-registered IRB without unnecessarily penalizing clinical investigators or sponsors who have attempted to follow the regulation in good faith.

- FDA has requested feedback to the question, "Are additional changes to FDA regulations necessary?" PhRMA believes that no additional regulations are necessary. Existing regulations clearly define the obligation of sponsors and investigators to ensure review by IRBs that comply with the requirements of 21 C.F.R. Part 56. Therefore, additional regulations are not necessary nor would they increase compliance necessarily. Rather, PhRMA suggests that FDA use resources to promote awareness and compliance to these regulations through communications and industry/agency interactions.

In conclusion, PhRMA reiterates its support of the IRB registration system, and we thank you for your consideration of these comments.

Sincerely,